REMARKS

The Specification at page 9, lines 9-12, has been amended by correcting the punctuation. No new matter has been introduced by way of this amendment.

Claims 1, 6, and 10 have been amended to specify that the claimed retinoids are retinyl esters, retinol, retinal, or mixtures thereof. Support for this subject matter may be found in the Specification, page 4, lines 1-6.

Claim 6 has been further amended to specify the preferred range of retinoid, at about 0.01 to about 1 %. Support for this amendment may be found in the Specification, p. 5.

The present invention is directed to a new and unobvious combination of retinoids and retinoid boosters. The retinoid/retinoid booster combinations are maintained in separate compartments of a package and the retinoid composition is kept out of contact with oxygen to promote its stability.

Claim Rejections - 35 USC § 112

35 U.S.C. 112, first paragraph

The Specification Provides Enablement for "Retinoid Boosters"

Claims 1-15 were rejected under 35 U.S.C. 112, first paragraph, because the specification, according to the Office Action,while enabling for the particular compounds listed in tables B1-B5 of the specification, does not reasonably provide enablement for "retinoid boosters" in general.

Applicants traverse this rejection and respectfully submit that the Specification is enabling for all the retinoid boosters claimed. The claims are commensurate in scope with the retinoid boosters as defined in the Specification. Retinoid boosters are defined in the Specification as compounds that inhibit or enhance the activity of certain enzymes which drive the equilibrium of the retinoid metabolism reaction shown in Chart 1. See Specification , page 5. It is believed that retinoids are enzymatically converted in the skin into retinoic acid according to the mechanism described in Chart 1. Retinoic Acid is the form of retinoid in the mechanism that Applicants strive to achieve. On the other hand, the equilibrium of the mechanism tends toward retinyl ester as the most stable form of retinoid. Therefore, Applicants have introduced compounds that would tend to drive the equilibrium of the mechanism toward the retinoic acid form. For example, B1 compounds are those that inhibit the ARAT/LRAT enzymes, so

that the equilibrium would shift in the direction of retinoic acid; B2 compounds are those that boost the activity of the Retinol dehydrogenase enzyme; B3 booster compounds are those that inhibit the activity of the Retinal reductase enzyme; etc. See also Specification, page 7, lines 1-14. Applicants have introduced in great detail the assays used to determine the activity of such retinoid booster compounds.

Criteria Used To Identify a Retinoid Booster Are Set Forth in the Specification hold on

The specification was objected to under 35 U.S.C. 112, first paragraph, as failing to adequately teach how to make and/or use the invention, and thereby failing to provide an enabling disclosure.

According to the Office Action, Applicant fails to set forth the criteria that defines "a retinoid booster"; Additionally, Applicant fails to provide information allowing the skilled artisan to ascertain these compounds, i.e., retinoid boosters, without undue experimentation; In the instant case, a number of "retinoid booster" examples are set forth in tables B1-B5, however, there is no explanation as to what common feature exists among the named examples; It is noted that these examples are neither exhaustive, nor define a particular class of compounds required; What common feature among these compounds exists?; Given the wide spectrum of compounds that are represented by the lists provided in Tables B1-B5,

e.g., fragrances, flavonoids, different acids, how would the skilled artisan be able to ascertain that a certain compound is a retinoid booster.

Applicants respectfully submit that the criteria that define "a retinoid booster" are set forth in the Specification. "Retinoid booster" is not a term found in the prior art, but is a term coined by the Applicants. Accordingly, Applicants are hereby exercising their right to be their own lexicographers by defining the term in the present Specification.

Applicants have set forth criteria allowing the activity of each embodiment to be individually assessed. A retinoid booster is defined as at least one compound that alone or at a combined concentration of 1 mM inhibits transglutaminase in an in vivo transglutaminase assay to more that 50 %. See, e.g., Specification, page 7, lines17-19. Applicants have provided information allowing the skilled artisan to ascertain retinoid boosters without undue experimentation. The common features among each set of boosters, i.e., each B1, B2, B3, etc., are defined as the assay a compound must pass in order to qualify as such a booster. See, e.g., Specification, page 8, lines 19-29; page 9, lines 9-12 and *infra*. For instance, B1 retinoid booster compounds are identified by the assay described in Section 2.3 of the Specification (pp. 12 – 13); B2 booster compounds are identified by the assay described in Section 2.4 of the Specification (pp. 14-15); B3 boosters are identified by the assay described in Section 2.5 of the Specification (p. 15); B4 boosters are identified by the

assay in Section 2.6 of the Specification (pp. 15-19); B5 boosters are identified by assay in 2.7 of the Specification (pp. 21); etc. Accordingly, the Specification provides sufficient guidance to the skilled artisan to ascertain, for each embodiment, whether a certain compound is a retinoid booster.

35 U.S.C. 112, second paragraph

Claims 1-15 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. According to the Office Action, the expression "retinoid booster" is indefinite; It is not clear which activities of the retinoid compound are boosted by these retinoid boosters.

Applicants respecfully traverse this rejection. As stated above, the term "retinoid boosters" is sufficiently defined in the Specification, making it clear which retinoid compounds are being boosted by way of boosting or inhibiting the enzymes that promote given reactions in the retinoid metabolizm Chart.

Claims 5, 10 and 15 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

According to the Office Action, the expression "mimicking the effect on skin of retinoic acid" is vague and indefinite.

Claims 1, 6, and 10 have been amended to recite specific retinoids, excluding retinoic acid. Applicants respectfully submit that the claims are now clear to the effect that a combination of a claimed retinoid and booster mimick the effects of retinoic acid. The effects of retinoic acid are described in detail throughout the Specification.

The Term "Stable" Has Been Properly Defined

According to the Office Action, the term "stable" in claim 1-3, 6-8 and 11-13 is a relative term which renders the claims indefinite; the term "stable" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

not defined

Applicants respectfully submit that the term "stable" has been properly defined in the specification. See, for instance, the Example on pp. 36-37, which discusses the reduced stability of retinol against degradation in the presence of boosters. In another instance, the Specification defines that retinoids, as well as combinations of retinoids and boosters, are generally unstable and may undergo chemical degradation, i.e., chemical instability.

See page 30, lines 11-14. Retinoid compositions are prone to degradation in the presence of oxygen. See Specification, page 31, lines23-24.

Claim Rejections - 35 USC § 103

Claims 1-15 were rejected under 35 U.S.C. 103(a) as being unpatentable over Suares et al. (USPN 5,914,116) in view of Katzung and Remington.

According to the Office Action, Suares et al. (USPN 5,914,116) teaches a method for a skin treatment comprising a topical application regime and a respective product; The product includes a first composition containing at least one active (0.10% Vitamin A palmitate),and a second composition including a second active (0.30% fragrance, and 3.00% stearic acid); The first and second compositions are stored in respective separate containers which are joined together, see col. 7 and 8, Example 1, col. 11, lines 32-36, and abstract in particular; Suares et al. also teaches that coumarines, hydroxycarboxylic acids (including hydroxyoctadecanoic acid), ceramides, phospholipids, linoleic acid, arachidic acid, phospholipidsimidazolidinyl urea are useful in its compositions.

The Office Action admits that Suares et al. (USPN 5,914,116) does not teach that the first and/or second compartments keep the respective compositions out of contact with oxygen, neither does it teach that the two

compartments are made of aluminum. However, Katzung is cited to remedy the deficiency for its teaching that retinoic acid is easily oxidized, page 940.

Applicants traverse this rejection and respectfully submit that Katzung does not remedy the deficiency of Suares et al. Firstly, Katzung merely restates the problem. Katzung merely states an invitation to invent. Secondly, the combination of Suares et al. and Katzung does not constitute an invention, and does not arrive at the subject matter of the present invention as claimed in Claim 1, as amended. Claim 1 excludes retinoic acid from among the retinoids because the compositions of the present invention are not intended to contain retinoic acid itself. Rather the compositions of the present invention would contain retinoids (of Chart 1) excluding retinoic acid. The required stability is not that of retinoic acid. Accordingly, Katzung does not remedy the deficiencies of Suares et al.

According to the Office Action, Remington in a subsection entitled "pharmaceutical containers" in the chapter on stability of pharmaceutical products teaches that aluminum containers are widely used in the pharmaceutical products.

Even if there were motivation to combine Remington with Suares et al. and Katzung, Remington only potentially affects the dependent claims of the present invention, i.e., those specifying that the preferred oxygen impermeable material is aluminum. However, there is not motivation to

combine Reminton with Suares et al. and Katzung because Remington deals with high temperature storage. High temperature storage is not relevant to the present invention. Again, even if combined, Applicants respectfully submit that, since the independent claims are in condition for allowance, those claims that depend from them are also in condition for allowance.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned **"Version With Markings To Show Changes Made."**

In view of the foregoing amendment and comments, applicants request the Examiner to reconsider the rejection and now allow the claims.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

The Specification at page 9, lines 9-12, has been amended as follows.

A booster is a compound which passes an in vitro Microsomal Assay described below in sections 2.1 through 2.7. A compound of the present invention inhibits or enhances at a concentration listed in Table A~~,~~ ~~A~~ an enzyme, to at least a broad % listed in Table A.

In the claims:

Claims 1, 6 and 11 have been amended as follows.

1. (Amended) A stable skin care product comprising:

a first composition comprising about 0.001% to about 10% of a retinoid selected from the group consisting of retinyl esters, retinol, retinal, and mixtures thereof;

a second composition comprising about 0.0001% to about 50% of at least one retinoid booster;

a first compartment for storing the first composition, wherein the first compartment keeps the first composition out of contact with oxygen; and

a second compartment for storing the second composition, the first and second compartments being joined together.

6. (Amended) A stable skin care product comprising:

a first composition comprising about ~~0.001~~ 0.01% to about ~~10~~ 1% of a retinoid to provide a first benefit;
said retinoid selected from a group consisting of retinyl esters, retinol, retinal, and mixtures thereof;

a second composition comprising about 0.0001% to about 50% of at least one retinoid booster to boost the first benefit;

a first compartment for storing the first composition, wherein the first compartment keeps the first composition out of contact with oxygen; and

a second compartment for storing the second composition, the first and second compartments being joined together.

11. (Amended) A stable skin care product comprising:

a first composition comprising about 0.001% to about 10% of a retinoid to provide a first benefit;

said retinoid selected from a group consisting of retinyl esters, retinol, retinal, and mixtures thereof;

a second composition comprising about 0.0001% to about 50% of at least one retinoid booster to boost the first benefit;

a first compartment for storing the first composition, wherein the first compartment keeps the first composition out of contact with oxygen; and

a second compartment for storing the second composition, wherein the second compartment keeps the second composition out of contact with oxygen; and wherein the first and second compartments are joined together.